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Re

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/181,601	10/29/98	ANDERSON	S 06137-0021-U
<input type="checkbox"/>		HM12/0723	<input type="checkbox"/> EXAMINER FREDMAN, J
<input type="checkbox"/>			<input type="checkbox"/> ART UNIT 1655
<input type="checkbox"/>			<input type="checkbox"/> PAPER NUMBER 21
DATE MAILED: 07/23/01			

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/181,601	ANDERSON ET AL.
	Examiner	Art Unit
	Jeffrey N Fredman	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) Responsive to communication(s) filed on 04 June 2001.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-17 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - a) All
 - b) Some *
 - c) None of the CERTIFIED copies of the priority documents have been:
 1. received.
 2. received in Application No. (Series Code / Serial Number) _____.
 3. received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) <input type="checkbox"/> Notice of References Cited (PTO-892)	17) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
15) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	18) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
16) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____	19) <input type="checkbox"/> Other: _____

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DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Wallace et al (Protein Science (June 1996) 5:1001-1013).

Wallace teaches a method for determining a biochemical function of a protein or polypeptide domain of unknown function (abstract) comprising: a) identifying a putative polypeptide domain that properly folds into a stable polypeptide domain having a definite three dimensional structure, b) determining the three dimensional structure of the stable polypeptide domain (page 1004-5, subheading "derivation of 3D templates"), c) comparing the determined three dimensional structure to known three dimensional structures in the protein data bank, wherein said comparison identified known homologous three dimensional structures (page 1009, subheading "search for Ser-His-Asp triads in other PDB entries"), d) correlating a biochemical function corresponding to the identified homologous structure to a biochemical function for the stable polypeptide domain (page 1009, figure 5 and page 1011, columns 1 and 2).

The claim does not require that the determination of three dimensional structure occur by a physical step, but broadly includes determinations which simply occur inside the computer algorithm, such as those taught by Wallace.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5-9, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace in view of Friedrichs et al (J. Biomol. NMR (1994) 4:703-726).

Wallace teaches the limitations of claims 1, 11 and 13 as discussed above. Wallace determines the three dimensional structure of the stable domain by reference to the protein database. Wallace does not teach NMR characterization of the protein nor automated NMR assignments.

Friedrichs teaches determination of the correctness of a protein structure using a variety of NMR spectrometer spectra (page 705) and automated analysis of these spectra using a

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computer program (pages 708-715). Friedrichs further teaches amide hydrogen exchanges (pages 705 and 708).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the 3-D structural alignment and function determination method of Wallace with the use of NMR structural determination of Friedrichs since Wallace states “This suggests that the development of databases of 3D templates, such as those that currently exist for protein sequence templates, will help identify the functions of new protein structures as they are determined and pinpoint their functionally important regions (abstract)”. Here, Wallace expressly motivates the determination of new protein structures. Motivation to use NMR in this determination is provided by Friedrich, who states “The choice of NMR experiments was based on considerations regarding the sensitivity and resolution of spectra for medium to large-sized proteins (page 720)”. Friedrich further motivates the automated assignment of NMR spectra in this determination, noting “Instead of taking weeks, the backbone assignments can be made in one or two days following data acquisition and processing (page 722)”. An ordinary practitioner would have been motivated to utilize NMR to determine protein structures in order to sensitively and accurately provide data for 3D determinations and would have been motivated to utilize the automated assignments of Friedrichs in order to minimize the time needed to determine the 3D structure as expressly motivated by Friedrichs.

Claims 1-9, 11, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace in view of Friedrichs and further in view of Farber et al (J. Mol. Biol. (1992) 226:471-479).

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Wallace in view of Friedrichs teach the method of claims 1, 5-9, 11 and 13 as discussed above. Wallace in view of Friedrichs does not teach a prestep of parsing a database to identify the protein coding regions.

Farber teaches a method of discriminating open reading frames (abstract and pages 472-474).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Wallace in view of Friedrichs with the database preparation method of Farber since Farber notes “Simple neural networks predict coding regions in DNA very well when trained on a representation of DNA using single codon frequencies (page 478, column 1)”. An ordinary practitioner would have been motivated to combine the method of Wallace in view of Friedrichs with the protein coding determinations of Farber in order to maximize the usable databases to identify homologous proteins and thereby determine the function of unknown proteins.

Claims 1, 5-11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace in view of Friedrichs and further in view of Bagby et al (J. Biomol. NMR (1997) 10:279-282).

Wallace in view of Friedrichs teaches the limitations of claims 1, 5-9, 11 and 13 as discussed above. Wallace in view of Friedrichs do not teach the button test for microdialysis and NMR.

Bagby teaches a method for preparing samples for NMR to determine optimal solubilization comprising the steps: a) preparing an array of microdialysis buttons with 5 μ l

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containing at least 1 mM protein (page 280), b) dialyzing each member of the array against a different buffer (page 280), c) analyzing the sample to determine if the protein remained soluble (page 280) and d) selecting the optimum solubility for NMR (page 280). Bagby expressly notes a lab expressed the desired protein (page 281, column 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the button test of Bagby with the NMR and functional determination method of Wallace in view of Friedrichs since Bagby states "The button test is an efficient, small scale way of tackling this problem.(page 281, column 1)". An ordinary practitioner would have been motivated to utilize the button test to optimize solubility for NMR since it is expressly noted as efficient and small scale, which reduced time and wasted reagents, which for purified proteins can represent a large investment of time and money.

Claims 1-9 and 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace in view of Friedrichs and further in view of Farber et al (J. Mol. Biol. (1992) 226:471-479) and further in view of Orengo et al (Structure (August 1997) 5:1093-1108).

Wallace in view of Friedrichs and further in view of Farber teach the method of claims 1-9, 11, 13 and 14 as discussed above. Wallace in view of Friedrichs and further in view of Farber does not teach the use of CATH to classify the protein domains.

Orengo teaches the use of CATH to classify the protein domains (abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the CATH method of Orengo with the NMR and functional determination method of Wallace in view of Friedrichs and further in view of Farber since

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Orengo states "A database of well-characterized protein structure families, such as CATH, will facilitate the assignment of structure-function/evolution relationships to both known and newly determined protein structures (abstract)". An ordinary practitioner would have been motivated to utilize CATH in the assignment of the protein structure in order to further enhance the specificity and sensitivity of the 3D structure-function determination, as expressly motivated by Orengo.

An ordinary practitioner would have been motivated to combine the reagents, software and apparatus used in the methods of Wallace in view of Friedrichs and further in view of Farber and further in view of Orengo into an integrated system for determination of protein function from protein structure in order to simplify the determination of protein function by collecting reagents of use in an obvious method into a single location to improve ease of use and minimize effort.

Response to Declaration

1. The Declaration under 37 CFR 1.132 filed June 4, 2001 is insufficient to overcome the rejection of the claims based upon 35 U.S.C. 103 as set forth in the last Office action because:

The declarant wishes to distinguish between domains of three amino acids, which he deems to be the domains of Wallace and domains of 50-100 amino acids of the claimed method. However, this argument is not directed toward the claim as it actually reads. Claim 1 states "(A) identifying a putative polypeptide domain that properly folds into a stable polypeptide domain of 50 to 300 amino acids". The declarant argues that the examiner is confusing the numbering of the amino acids with the determination of how many amino acids have been identified.

However, this argument fails to read the claims in their broadest reasonable interpretation. The claims, as broadly interpreted, read on identifying any polypeptide domain,

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that upon folding forms a stable domain of 50-300 amino acids. The Wallace domain, whether 3 amino acids or more, in order for proper folding requires and inherently folds into a stable polypeptide domain with comprises the entire polypeptide, or at least 195 amino acids. Thus, reading the claim using the Wallace reference as read by Declarant yields, '(a) identifying the putative triad polypeptide domain that properly folds into a stable polypeptide domain comprising the entire protein which is within the range of 50 to 300 amino acids'. This reading still indicates that Wallace anticipates this claim.

Response to Arguments

1. Applicant's arguments filed June 4, 2001 have been fully considered but they are not persuasive.
2. Applicant first argues that Wallace does not teach identification of a protein domain since the specification indicates that a protein domain generally involves 50 to 300 amino acids. This argument has already been addressed above in the response to the Declarant. Applicant should note that, absent a secondary consideration, there is also no evidence as to why selection of 50 amino acid domains would be unobvious over shorter domains. Such evidence of a secondary consideration might, if persuasive, be dispositive of an amended claim that overcame the 102 rejection. Each reference is cited to provide some of the teachings as discussed in the rejections above.

Conclusion

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeff Fredman, Ph.D. whose telephone number is (703) 308-6568.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CMC Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).



Jeffrey Fredman
Primary Patent Examiner
Art Unit 1655

October 1, 1999